Neuronal Control of Breathing

I Breathing Kinematics

- Spirometry is used to assess lung volumes and is helpful to classify lung diseases as obstructive or restrictive.
- Erythrocyte pulmonary capillary transit time is helpful to understand diffusion of gasses across the alveolar-capillary membrane.
- Oxyhemoglobin Dissociation curves are used to evaluate the oxygen transport.
- Pressure resistance graphs show the effect of PAP on pulmonary vascular resistance.
- Lung volume plotted against total pulmonary vascular resistance shows FRC as the lowest resistance as it is the balance between alveolar and extra alveolar vessel resistance.
- Pressure volume curves demonstrate the compliance of the lung (C=Change in V/Change in Pressure)
- Maximum Expiratory Flow Volume Curves show the effort dependent and independent and the peak flow of pulmonary ventilation.

Realize that the apex of the lung has the highest pO2, the lowest hydrostatic pressure, lowest intrapleural pressure, the highest alveolar volume and the lowest compliance. The base is the exact opposite and has the highest hydrostatic pressure with the highest intrapleural pressure, the lowest alveolar and the highest compliance.

II Nervous System Control

Inspiration requires inspiratory muscles to contract and draw air in through the generation of increasingly negative intrapleural pressures. There is a latent period of a few seconds followed by an inspiratory ramp with a crescendo effect to create a smooth inhalation decreasing turbulence. Expiration is usually passive and the result of elastic recoil. Expiration has two stages: marked decrease in firing potential (stage 1) and complete cessation of action potentials (stage 2). This causes the smooth sinusoidal mechanical expiration. The deeper you inhale the more motor units your brain has to recruit.

Respiratory control can be divided into the voluntary control center, the automatic control center and the spinal cord center. Reflexes utilize these centers to stimulating respiration.

Automatic control of breathing

The periodic nature of breathing is controlled by pattern generator ganglia in the medulla/pons

1. Medulla: Respiratory center that initiates inspiration
    a. **Pre-Botzinger complex**: Pacemaker cells in the retrofacial nucleus **RF**
    b. Dorsal Respiratory group DRG: Inspiratory neurons in the ventrolateral nucleus of the tractus solitaries **vl-NTS** to the contralateral phrenic
    c. Ventral respiratory group VRG: Expiratory and inspiratory neurons in the nucleus retroambigualis **NRA** to contralateral side

2. Pons: Control center with refinement
    a. **Apneustic center:** caudal, promotes inspiration by decreasing rate and increasing depth
    b. **Pneumotaxic center PRG:** rostral and caudal to the inferior colliculus. Nucleus Parabrachialis medialis **NPBM** and Kolliker-Fuse nucleus **KF** with inspiratory and expiratory neurons. These decrease inspiration and increase expiration

*****NOTE: The two major "Cut-off switches" for breathing are the Pneumotaxic center and the vagus. Loss of either results in decreased rate increased depth. Loss of both causes apneusia (no breaths after inspiration) since the apneustic center fires AP without inhibition.*****

Voluntary Control of Breathing

Cerebral cortex is responsible for overriding the brainstem to stimulate breathing. Limbic and Hypothalamus can also play a role in initiating breathing

Chemical Control

There are peripheral and central chemoreceptors that play a primary role in initiating respiration

1. Peripheral: include the carotid bodies (glomus assesses PO2, PCO2, pH **CNIX**) and the aortic arch (multiple scattered along the arch to monitor the PO2 and PCO2 **CNX**)
2. Central: Ventrolateral medulla near the CNIX and X exit from the brainstem. Increases in extracellular fluid and CSF [H+] is due to the increase in CO2 being converted to bicarb and H+. This contributes ~80% of respiratory drive. The decrease in pH causes stimulation of the medullary respiratory center to increase ventilation. Low PO2 and systemic pH provide synergistic effects increasing RR.

CO2 response curve decreases as we age, sleep, COPD, narcotics and anesthesia. When PaCO is chronically elevated, the brain will attempt to restore pH by transport of HCO3 from the blood into the medulla and CSF removing the central hypercapnic drive to increase respiration. Hypoxic drive will take over as the primary motivator to breathe. *****NOTE: Oxygen induced hypoventilation: the result of increased FiO2 after a prolonged state of hypercapnia will remove the hypoxic drive currently stimulating the respiratory center to breathe. The hypercapnia will increase since: O2 induced hypoventilation, increased V/Q mismatch since reversal of hypoxic pulmonary vasoconstriction, Haldane effect with CO2 unloading of hemoglobin to bind the new O2. Hypoxic drive=<50-60mmHg PaO2**

Metabolic acidosis will stimulate hyperventilation almost entirely by the action of the carotid bodies. Hydrogen ions may cross the BBB but too slowly to stimulate the central chemo receptors.

Reflexes

1. Pulmonary stretch receptors: lung inflation stimulates pulmonary stretch receptors which in turn act to terminate inspiration and decrease the respiratory rate. **Herring-Breuer Inflation Reflex** is mediated by impulses utilizing the vagus nerves and originates from slow adapting stretch

receptors in the SMC of the large bronchi and bronchioles. They have tonic activity and only after inhalation of +1L do their activities actually become large enough to trigger the reflex. **Herring-Breuer Deflation Reflex** is mediated by impulses in the vagus nerve that are triggered similar stretch fibers by lung deflation and trigger tachypnea

2. Irritant airway receptors: chemicals and irritants stimulate rapidly adapting receptors in the epithelium to stimulate afferent efferent vagal nerves causing cough, bronchoconstriction and mucus secretion. Hyperreactivity asthma is thought to have something to do with this pathway.
3. Juxtapulmonary receptors: are located in the walls of the pulmonic capillaries such that increases in the volume or pressure of the vessels or interstitial space will trigger these receptors to active vagal unmyelinated C fibers… results in tachypnea and dyspnea.
4. Joint proprioception: stimulation activates afferent fibers in the spinal cord to increase the rate and depth of breathing
5. Muscle spindle reflex: similar in that muscle stretching will utilize spinal pathways to increase the TV by increasing respiratory muscle contraction when the chest wall compliance is decreased
6. Baroreceptors: exert a small influence on ventilation. Hypertension elicits brief apnea while hypotension causes tachypnea.
7. Pain receptors: somatic pain stimulates newborns to breathe and use various spinal pathways. Visceral pain triggers apnea.
8. Integrated reflexes of Exercise: minute ventilat8ion increases linearly with O2 consumption and CO2 production up to 60% of the body's maximal work capacity with **exercise hyperpnea (central command, joints, thermo, mechano, metabolic inputs)**. PCO2 is normal at workloads less than this anaerobic threshold. Once the threshold is reached, the increase in lactate causes such a decrease in the pH that the metabolic acidosis will stimulate respiratory compensation of **hyperventilation**.

III Irregular breathing patterns

- **Apnea**: cessation of breathing at the end of expiration
- **Apneusis**: cessation of breathing at the end of inspiration
- **CheyneStokes breathing**: crescendo/decrescendo breathing interrupted by periods of apnea (high altitude, sleep, heart/brain damage)
- **Yawning**: normal response to fatigue due to a vasovagal reaction most likely (not a gas exchange). Seen to increase with lower temps
- **Hiccups**: due to involuntary spasm of the diaphragm (actually a myoclonic seizure) due to large meal, sudden change in stomach temp, alcohol, smoking or sudden excitement. Cancer, stroke, injury can cause intractable hiccups due to irritation of the phrenic nerve. Chlorpromazine is an anitpsych drug used, metoclopramide and baclofen. Surgery can be used or a vagal nerve stimulator
- **Kussmaul breathing**: deep and labored associated with severe metabolic acidosis
- **Sleep apnea**: Intrinsic sleep disorder that is central or obstructive
- **Ondines curse**: central alveolar hyperventilation due to loss of automatic control